PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 42191	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/FI2005/050061	International filing date *(day/month/year)* 03-03-2005	Priority date *(day/month/year)* 05-03-2004

International Patent Classification (IPC) or national classification and IPC

See Supplemental Box

Applicant

Biohit Oyj et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of   **6**   sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of   **3**   sheets, as follows:

        ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

        ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

       _____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I   Basis of the report

   ☒ Box No. II   Priority

   ☐ Box No. III   Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

   ☐ Box No. IV   Lack of unity of invention

   ☒ Box No. V   Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   ☒ Box No. VI   Certain documents cited

   ☐ Box No. VII   Certain defects in the international application

   ☐ Box No. VIII   Certain observations on the international application

Date of submission of the demand 27-12-2005	Date of completion of this report 16-03-2006
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Form PCT/IPEA/409 (cover sheet) (April 2005)

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of: Cover sheet

International patent classification (IPC)

G01N 33/74   (2006.01)
G01N 33/573 (2006.01)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI2005/050061

Box No. I	Basis of the report

1. With regard to the **language**, this report is based on:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into _____ ,
   which is the language of a translation furnished for the purposes of:

   ☐ international search (Rules 12.3(a) and 23.1(b))

   ☐ publication of the international application (Rule 12.4(a))

   ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

   ☐ the international application as originally filed/furnished

   ☒ the description:

   pages   1-17 _____ as originally filed/furnished

   pages* _____ received by this Authority on _____

   pages* _____ received by this Authority on _____

   ☒ the claims:

   pages _____ as originally filed/furnished

   pages* _____ as amended (together with any statement) under Article 19

   pages*   18-20 _____ received by this Authority on   27-12-2005 _____

   pages* _____ received by this Authority on _____

   ☒ the drawings:

   pages   1-4 _____ as originally filed/furnished

   pages* _____ received by this Authority on _____

   pages* _____ received by this Authority on _____

   ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

   ☐ the description, pages _____

   ☒ the claims, Nos.   1-16 _____

   ☐ the drawings, sheets/figs _____

   ☐ the sequence listing *(specify)*: _____

   ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages _____

   ☐ the claims, Nos. _____

   ☐ the drawings, sheets/figs _____

   ☐ the sequence listing *(specify)*: _____

   ☐ any table(s) related to the sequence listing *(specify)*: _____

   * *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. II	Priority

1. ☐   This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

     ☐   copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

     ☐   translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐   This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3.   Additional observations, if necessary:

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The priority is considered valid.
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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-15		YES
	Claims			NO
Inventive step (IS)	Claims	1-15		YES
	Claims			NO
Industrial applicability (IA)	Claims	1-15		YES
	Claims			NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following document:

D1: WO 02/054084 A1

The document D1 is regarded as being the closest prior art to the subject-matter of amended claims 1-15, and shows methods for assessing the condition of the gastric mucosa, such as to diagnose gastric changes in the mucosa. D1 contemplates determining the same markers, namely PGI, gastrin and a H. pylori marker.

However, D1 compares the measured marker concentrations with a predetermined cut-off value for the said marker, then forms a specific combination of such obtained comparison results and, based on this combination, it makes a diagnosis.

The subject-matter of amended claims 1-15 in the present application concerns a method based on quantification of a prediction. Therefore differs from this known method in D1 in that the probability is analyse for defined gastric mucosa classes in order to make a diagnosis. The subject-matter of claims 1-15 is therefore novel (Article 33(2) PCT).

-The problem to be solved by the present invention may therefore be regarded as improved methods for detecting gastric mucosa diseases.
-The solution to this problem proposed in amended claims 1-15 of the present application is considered as involving an inventive step (Article 33(3) PCT).

Box No. VI   Certain documents cited

1. Certain published documents (Rule 70.10)

	Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
P,A	US6696262B2	24.02.04	14.03.01	15.11.95
P,X	WO2004/023148	18.03.04	05.09.03	06.09.02

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Claims

1. Method for assessing or predicting the state of the gastric mucosa in a subject by determining, in said subject, the probability for the gastric mucosa belonging to at least one gastric mucosa class, the method comprising

   - measuring, from a sample of said subject, the pepsinogen I (PGI) and gastrin-17 (G-17) analyte concentrations, as well as determining the presence or concentration of a marker for *Helicobacter pylori*,

   - entering the data so obtained in a data processing system comprising an operating system, a database and means for transceiving and processing data, the said data processing system being adapted to determine the probability for the gastric mucosa belonging to the at least one gastric mucosa class, the gastric mucosa class being selected from the group of classes consisting of normal (N), antrum atrophy (A), antrum and corpus atrophy (AC), corpus atrophy (C) and superficial or non-atrophic gastritis (S), based on the data entered as well as on predefined clinical data in the database, the information so generated by the data processing system being indicative of the state of the gastric mucosa in said subject.

2. The method according to claim 1 for assessing a change in the state of the gastric mucosa, the method comprising repeating the determination of the probability for the at least one gastric mucosa class, and comparing the probabilities so obtained with the earlier determined probabilities in order to provide information relating to the change in the state of the gastric mucosa.

3. The method according to any one of the preceding claims, wherein the predefined clinical data in the database comprises data obtained from a reference population group by gastroscopic study and determination of the PGI and G-17 analytes and *Helicobacter pylori* marker in said reference population group.

4. The method according to any one of the preceding claims wherein the probabilities are determined using a statistical method for calculation of the classification probabilities.

5. The method according to claim 4 wherein the statistical method for the calculation of the classification probabilities is a multinominal logistic regression method (MLR).

6. The method according to any one of the preceding claims, comprising the further step of using the generated information for providing a diagnosis and/or a suggestion for further treatments or examinations.

7. The method according to any one of the preceding claims, wherein the *Helicobacter pylori* marker is a *Helicobacter pylori* antibody, the concentration of which is measured from the sample.

8. The method according to any one of the preceding claims, wherein the *Helicobacter pylori* marker is the *Helicobacter pylori* antigen, the presence of which is determined in the sample.

9. The method according to any one of the preceding claims, wherein the gastrin value measured is the stimulated gastrin-17 value (G-17st), or both the gastrin-17 and the stimulated gastrin-17.

10. The method according to any one of the preceding claims, wherein, in addition, the concentration of the analyte pepsinogen II (PGII) is measured, and the ratio PGI/PGII is used in the statistical calculation.

11. The method according to claim 1, wherein the analytes are measured from a body fluid, such as a serum whole blood, urine, saliva or lacrimal fluid sample, especially a serum sample.

AMENDED SHEET

12. The method according to any one of the preceding claims, wherein the data processing means comprise a display, and the information generated is displayed on the display.

13. A kit comprising means for determining, from a sample, the pepsinogen I and gastrin-17 concentration, and the concentration or presence of a *Helicobacter pylori* marker, as well as a computer program product embodied on a computer readable medium and comprising computer code means adapted to determine a probability for a gastric mucosa class, the gastric mucosa class being selected from the group of classes consisting of normal (N), antrum atrophy (A), antrum and corpus atrophy (AC), corpus atrophy (C) and superficial or non-atrophic gastritis (S), based on measured values for said analytes and/or marker as well as predefined clinical data in a database, and to provide information in response to said determination and optionally other entered data, when run on a computer.

14. The kit according to claim 13, wherein the predefined clinical data comprises data obtained from a reference population group by gastroscopic studies and determination of values for PGI and G-17 analytes and *Helicobacter pylori* marker from said reference population group.

15. A computer program product embodied on a computer readable medium and comprising computer code means adapted to determine a probability for a gastric mucosa class, the gastric mucosa class being selected from the group of classes consisting of normal (N), antrum atrophy (A), antrum and corpus atrophy (AC), corpus atrophy (C) and superficial or non-atrophic gastritis (S), based on measured values for the PGI and G-17 analytes and *Helicobacter pylori* marker, as well as predefined clinical data in a database, and to provide information in response to said determination and optionally to other entered data, when run on a computer.

AMENDED SHEET